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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/753,261	01/07/2004	Jane Daun	9626-9IPX	6698

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PO BOX 37428
RALEIGH, NC 27627

EXAMINER

DESAI, RITA J

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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07/16/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/753,261	Applicant(s) DAUN ET AL.	
	Examiner Rita J. Desai	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/07</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

In view of the papers filed May 10 2004, the inventorship in this nonprovisional application has been changed by the deletion of

Heather A. Davis, Haverhill, MA, USA
Bruce DeCosta, Salem, Nit, USA
Fabian Gusovsky, Andover, MA USA
Ieharn Hishinuma, Ibaraki, JAPAN
Yimin Jiang, Londonderry, NH USA
Toshihiko Kaneko, Ibaraki, JAPAN
Kouichi Kikuchi, Ibaraki, JAPAN
Andre Lescarbeau, Somerville, MA USA
Xiang-Yi Li, Andover, MA USA
Kenzo Muramoto, Ibaraki, JAPAN
Norihito Ohi, Ibaraki, JAPAN
Marc Pesant, Andover, MA USA
Boris M. Seletsky, Andover, MA USA
Motohiro Soejima, Ibaraki, JAPAN
Lynda Tremblay, Tewksbury, MA USA
Ye Yao, North Andover, MA USA
Hiromitsu Yokohama, Ibaraki, JAPAN
Yan Zhao, North Andover, MA USA
Wanjun Zheng, Londonderry, NH USA

The BIB data sheet reflects the correct inventors.

Accordingly, the persons named as the co-inventors of the subject application are
Jane DAUN, of Dracut, Massachusetts;
Scott FIELDS, of Towaco, New Jersey; and
Seiichi KOBAYASHI, of Belmont, Massachusetts.

The IDS filed 3/26/07 has been reviewed.

The rejection of claims 1-28 and the new claims 29-35 under 35 USC 112 still stands.

The rejection is being repeated here.

The specification does not enable any physician Skilled in the art of medicine, to make and use the invention commensurate in scope with these claims. The how to make and use requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed

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process work. "The eight factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The main issues are the correlation between clinical efficacy for treatment of reperfusion injuries, osteoporosis and/or bone metastasis and Applicants' assay @ paragraph 0369 in the PG Pubs. a) Determining if any particular claimed compound would treat any particular disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases – reperfusion

The direction concerning treating the named diseases is found beginning @ paragraph 100, which merely states Applicants' intention to do so. Applicants describe formulations @ paragraph 117. Doses required to practice their invention are described beginning @ paragraph 151. Since none of the compounds have ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these different diseases? There are no guidelines for determining the doses needed to provide an osteoporosis effect vs. a bone metastasis effect vs. a reperfusion injury effect. Are the identical doses to be used for treating these unrelated diseases? There is an assay described @ paragraph 369 with no data but it is unclear if this assay is correlated to claimed diseases. The issue of "correlation" is related to the issue of the presence or absence of working examples. "Correlation" as used herein refers to the relationship between in vitro or in vivo animal model assays and the disclosed/claimed method of use. An in vitro or in vivo animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. The instant application contains no such animal model or example, therefore there is no correlation and the examples do not constitute "working examples." Otherwise applicants just state @ paragraph 117 the compounds may be assayed using known assays. c) There is no working example of treatment of any disease in man or animals. The assay provides IC₅₀ values for the present compounds. However, this value does not equal to effective treatment of the claimed diseases, d) The nature of the invention is clinical treatment of the claimed disease with the claimed compounds, which involves physiological activity, e) The state of the clinical arts in claimed diseases is high.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience, g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain), h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the diseases embraced by the claim. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

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Applicants are arguing that other documents have claims that have similar activity.

All the compounds in the prior art are not similar. Applicants should know that pharmaceutical art is highly unpredictable.

The state of the prior art: The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group versus a hydrogen changes the properties altogether. A good example is a theophylline versus caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Testing involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment of reperfusion injuries and osteoporosis or bone metastasis as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Applicants diseases are so diversified, which includes osteoporosis and bone cancer !

The breadth of the claims: Applicants breadth of the claim is also at an issue here, and reduction to practice of making this large scope of compounds and then being able to "treat" these various diseases is at issue.

The nature of the invention: The invention is a complex compound that is useful to treat or lessening the severity of reperfusion injuries, osteoporosis and/or bone metastasis.

The level of one of ordinary skill: The ordinary artisan is highly skilled.

The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The level of unpredictability in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

Applicants diseases are very diversified and there is no correlation between them.

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The amount of direction provided by the inventor: There is no test data . Only HUVEC assay protocol.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome and UNDUE.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

“A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable.”

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

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Conclusion

Claims 1-35 stand rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
July 9, 2007

R. Desai
7/9/07